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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,792	04/13/2001	Robert F. Margolskee	34116/1051	8395

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MICHAEL L. GOLEMAN
NIXON PEABODY LLP
CLINTON SQUARE, P.O. BOX 31051
ROCHESTER, NY 14603

EXAMINER	
BRANNOCK, MICHAEL T	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 12/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/834,792	MARGOLSKEE ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *37-40* is/are allowed.

6)☒ Claim(s) *41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth on 9/25/2006, have been entered in full.

Response to Amendment

Applicant is notified that any outstanding objection or rejection that is not expressly maintained in this Office action has been withdrawn in view of Applicant's persuasive arguments and evidence. Specifically, regarding the outstanding 35 USC 101 utility rejection, a review of the literature reveals that the mouse trpm5 protein (the presumed ortholog of the instant human TRP8) is generally regarded in the art to be a component of a bitter taste transduction pathway in mice, see Chandrashekar-J et al., Nature 444(288-294)2006, see page 7 of the HTML print-out provided. The instant application has correctly prophesized this. Also, in the Declaration under 37 CFR 1.132, Robert Bryant demonstrates that mTRP8 is involved in bitter taste perception using TRP8 knock-out mice. One would thus expect that an assay that measures the effect of compounds on TRP8 activation, would then be useful for identifying compounds that induce the perception of bitter taste, as is currently claimed.

Regarding rejections under 35 USC 112, first paragraph: the specification apparently mischaracterizes the functional activity of TRP8. It is assumed that the functional experimentation provided in Example 6.2.5 of the specification utilizes mouse TRP8 (trpm5) and not the human TRP8 of SEQ ID NO: 4. In this example, the specification asserts that TRP8 is a store operated Ca^{2+} channel whose function requires external Ca^{2+} and can be induced through store depletion of Ca^{2+} using thapsigarin. These results appear to be published in Perez-CA et al., Nature Neuroscience 5(11)1169-1176, 2002. However, the art regarding the activity of

TRP8 (TRPM5) was, and is, controversial and contradictory to the conclusions presented in Perez and in the instant specification, see Liu and Liman, PNAS 100(15160-15160)2003 , bottom of col. 1 of 15164. Regarding Applicant's published work (Perez, supra) Liu and Liman state that "the conductance described in this report [that of Perez] does not resemble the TRPM5 currents that we recorded, either in rectification properties, Ca^{2+} permeability or sensitivity to La^{3+} block". Furthermore, we were unable to observe significant activation of TRPM5 by short-term thapsigargin treatment" see the top of col 1 of page 15164 and supplemental Figure 7 wherein robust currents are observed after the addition of a Ca^{2+}ionophore and no activity is observed after the addition of thapsigargin. Additionally, Prawitt-D et al., PNAS 100(25)15166-15171, 2003 find no evidence for a store-operated Ca^{2+} activation mechanism for TRPM5 and report that that TRPM5 is essentially impermeable to Ca^{2+}, see col 1 bridging col 2 of page 15166. Likewise, Hofmann et al., Current Biology, 13(1153-1158)2003 report that TRPM5 is a monovalent selective cation channel and not a Ca^{2+} channel, see the Abstract.

However, the claims have been amended to specify that the level of TRP8 activation is measured by measuring the membrane potential of the cell. Thus, strictly speaking, one would not need to know the correct conductance properties and characteristics of TRP8 to determine whether or not a compound altered the membrane potential of a cell expressing TRP8 and further determining that TRP8 was the cause of that change in potential, i.e. that the level of TRP activation was altered.

New Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 41 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 41 requires providing a nerve and operably linking the nerve to the cell and measuring the action potential of the nerve. There is no teaching in the specification of how this is to be done with an *isolated* cell expressing a human TRP8 and it does not appear to be recognized in the art. In Applicant's remarks of 4/7/2005, Applicant pointed to prior Application 60/197491, pages 25-26, in support of this claim (then claimed as claim 36). However, the examiner finds that this disclosure only relates to dissected nerve complexes in mice and does teach a step of operably linking a nerve to an isolated cell expressing a human TRP8.

Claim 41 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

the inventor(s), at the time the application was filed, had possession of the claimed invention. As set forth above, Claim 41 requires providing a nerve and operably linking the nerve to the cell and measuring the action potential of the nerve. There is no teaching in the specification regarding an *isolated* cell expressing a human TRP8 and the step of operably linking the cell to a neuron. This claim first appears in as an amendment to the claims in 4/7/2006 as claim 36. In Applicant's remarks of 4/7/2005, Applicant pointed to prior Application 60/197491, pages 25-26, in support of this claim (then claimed as claim 36). However, the examiner finds that this disclosure only relates to dissected nerve complexes in mice and does teach a step of operably linking a nerve to an isolated cell expressing a human TRP8, thus one of skill in the art would not recognize that Applicant was in possession of such at the time of filing, and introduction of such into the disclosure constitutes new matter.

Allowable Subject Matter

Claims 37-40 are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867. Official papers filed by fax should be directed to **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

December 9, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER